Background: Epigenetic modifications, which include DNA methylation, covalent histone modifications and non-coding RNA mechanisms, play important roles in regulation of gene expression. DNA methylation, in particular, has attracted attention as it relates to disease prevention and treatment. During carcinogenesis, tumor suppressor genes are methylated in their regulatory regions and silenced, whereas oncogenes lose methylation and become actively transcribed. In this study, we focus on enhancer regions, which are intensively studied gene regulatory regions, and investigate how dietary bioactive compounds, specifically resveratrol from grapes, change epigenetic makeup at enhancers of oncogenes and thereby attenuate cancer development.

Methods and Results: Human breast cancer cell lines, non-invasive MCF10CA1h, and invasive MCF10CA1a, were treated with resveratrol at 15 µM concentration for 9 days. The effect of the treatment on the DNA methylation patterns was determined using Illumina-450K methylation microarray. We found 1,751 and 1,803 differentially methylated CpG sites (0.05 ≥ differential methylation ≤ -0.05, p<0.05) located in enhancers upon resveratrol treatment in MCF10CA1h and MCF10CA1a cells, respectively, as compared with vehicle treated cells. Functions, biological processes, and signaling pathways of genes corresponding to differentially methylated sites were analyzed using bioinformatics tools. We further identified 103 genes that are hypermethylated targets in both breast cancer cell lines and discovered that majority of them are linked to oncogenic functions.

Conclusions: Our results confirm a potential role of dietary polyphenols in regulation of DNA methylation at enhancer regions which may result in silencing of genes with oncogenic functions and may contribute to anti-cancer action of these compounds.

Themes: Check (highlight) the most applicable theme according to the abstract.

| Innovation and Technology | Health and Wellness | Culture and Society | Sustainability and Conservation |

Comments: Very well written abstract. I have suggested that the author provide a hypothesis for the research as well as a statement at the end regarding future research or implications. Great work!